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## Advances in Pancreatic Islet Transplantation Sites for the Treatment of Diabetes.

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### Public Summary:

Diabetes is a complex disease that affects over 400 million people worldwide. The life-long insulin injections and continuous blood glucose monitoring required in type 1 diabetes (T1D) represent a tremendous clinical and economic burdens that urges the need for a medical solution. Pancreatic islet transplantation holds great promise in the treatment of T1D; however, the difficulty in regulating post-transplantation immune reactions to avoid both allogenic and autoimmune graft rejection represent a bottleneck in the field of islet transplantation. Cell replacement strategies have been performed in hepatic, intramuscular, omentum, and subcutaneous sites, and have been performed in both animal models and human patients. However more optimal transplantation sites and methods of improving islet graft survival are needed to successfully translate these studies to a clinical relevant therapy. In this review, we summarize the current progress in the field as well as methods and sites of islet transplantation, including stem cell-derived functional human islets. We also discuss the contribution of immune cells, vessel formation, extracellular matrix, and nutritional supply on islet graft survival. Developing new transplantation sites with emerging technologies to improve islet graft survival and simplify immune regulation will greatly benefit the future success of islet cell therapy in the treatment of diabetes.

### Scientific Abstract:

Diabetes is a complex disease that affects over 400 million people worldwide. The life-long insulin injections and continuous blood glucose monitoring required in type 1 diabetes (T1D) represent a tremendous clinical and economic burdens that urges the need for a medical solution. Pancreatic islet transplantation holds great promise in the treatment of T1D; however, the difficulty in regulating post-transplantation immune reactions to avoid both allogenic and autoimmune graft rejection represent a bottleneck in the field of islet transplantation. Cell replacement strategies have been performed in hepatic, intramuscular, omentum, and subcutaneous sites, and have been performed in both animal models and human patients. However more optimal transplantation sites and methods of improving islet graft survival are needed to successfully translate these studies to a clinical relevant therapy. In this review, we summarize the current progress in the field as well as methods and sites of islet transplantation, including stem cell-derived functional human islets. We also discuss the contribution of immune cells, vessel formation, extracellular matrix, and nutritional supply on islet graft survival. Developing new transplantation sites with emerging technologies to improve islet graft survival and simplify immune regulation will greatly benefit the future success of islet cell therapy in the treatment of diabetes.

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